

CLAIMS

We Claim:

- 5 1. A method for making a polysaccharide derivative comprising reacting an acyl donor and a polysaccharide to form an acyl ester of the polysaccharide in a reaction medium comprising an organic solvent in the presence of a hydrolytic enzyme.
- 10 2. The method of Claim 1 wherein the hydrolytic enzyme is a lipase or a protease.
3. The method of Claim 1 wherein the hydrolytic protease is a bacterial protease.
4. The method of Claim 1 wherein the hydrolytic protease is an alkaline protease.
- 15 5. The method of Claim 1 wherein the hydrolytic enzyme is subtilisin or Proleather.
6. The method of Claim 1 wherein the hydrolytic protease is a lyophilized protease.
- 20 7. The method of Claim 1 wherein the reaction medium solubilizes the polysaccharide.
8. The method of Claim 1 wherein the organic solvent solubilizes the polysaccharide and the acyl donor.
- 25 9. The method of Claim 1 wherein the solubility of polysaccharide in the organic solvent is at least about 1 g of polysaccharide per liter of solvent at 20°C.

10. The method of Claim 1 wherein the solubility of the polysaccharide in the organic solvent is at least about 10 g polysaccharide per liter of solvent at 20°C.
- 5 11. The method of Claim 1 wherein the organic solvent is selected from the group consisting of pyridine, dimethylformamide, morpholine, N-methylpyrrolidone and dimethylsulfoxide.
- 10 12. The method of Claim 1 wherein the reaction medium contains less than about 5% by volume water.
13. The method of Claim 1 wherein the reaction medium contains less than about 1% by volume water.
- 15 14. The method of Claim 1 wherein the reaction medium contains less than about 0.25% by volume water.
15. The method of Claim 1 wherein the reaction medium is anhydrous.
- 20 16. The method of Claim 1 wherein the polysaccharide is inulin or dextran.
17. The method of Claim 1 wherein the acyl donor comprises an acyl group and at least one enzymatically-cleaved group.
- 25 18. The method of Claim 17 wherein the enzymatically-cleaved group is a vinyloxy group.
19. The method of Claim 17 wherein the acyl donor is a polymerizable moiety.

20. The method of Claim 1 wherein the acyl donor is vinyl acrylate or methyl ester.
21. The method of Claim 1 wherein the acyl donor reacts with two molecules of polysaccharide.

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22. The method of Claim 1 wherein the acyl donor is divinyl adipate.
23. The method of Claim 1 wherein the polysaccharide has a molecular weight of at least about 700 Da.

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A method for making a polymer comprising reacting a polymerizable acyl donor and a polysaccharide in a reaction medium comprising an organic solvent in the presence of a hydrolytic enzyme thereby making a polysaccharide monomer and polymerizing the monomer, thereby making a polymer.

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The method of Claim 24 wherein the polysaccharide is inulin and the polymer is a hydrogel.

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The method of Claim 25 wherein the inulin polymer polymerizing step is a free radical polymerization.

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The method of claim 25 wherein the free radical polymerization is initiated by an initiator selected from the group consisting of potassium persulfate, hydrogen peroxide, azobisisobutyronitrile, benzoyl peroxide and tert-butyl peroxide.

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The method of Claim 25 wherein the polymerizing step is conducted in a reaction medium comprising an organic solvent.

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29. The method of Claim ²⁵ further comprising the step of removing the enzyme from the reaction medium.

5 30. The method of Claim ²⁵ wherein the polymerization is a dimerization.

31. The method of claim ²⁵ wherein the polymerizable acyl donor comprises two terminally located vinyl groups.

10 32. The method of Claim ²⁴ wherein the polysaccharide is characterized by a molecular weight of at least about 700 Da.

33. The method of Claim ²⁴ wherein the enzymatic esterification reaction is regiospecific.

15 34. The method of Claim ²⁴ wherein the Degree of Substitution is at least about 10%.

35. The method of Claim ²⁴ wherein the Swelling Ratio at Equilibrium is at least about 2.

20 36. The method of Claim ²⁴ wherein the average mesh size is between about 10 and 100 Å.

25 37. A polysaccharide derivative made by the method of Claim 1.

38. 39. A polysaccharide polymer made by the method of Claim ²⁴.

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39. A cross-linked inulin characterized by a Degree of Substitution of at least about 10%, a Swelling Ratio at Equilibrium of at least about 2 and an average mesh size between about 10 and 100 Å.

5 40. The cross-linked inulin of Claim 39 wherein inulin is cross-linked by a diester.

41. The cross-linked inulin of Claim 39 wherein inulin is cross-linked with a dimerized vinyl acrylate.

10 42. A pharmaceutical composition comprising an active agent and a cross-linked inulin characterized by a Degree of Substitution of at least about 10%, a Swelling Ratio at Equilibrium of at least about 2 and an average mesh size between about 10 and 100 Å.

15 43. The pharmaceutical composition of Claim 42 wherein the active agent is dispersed within the cross-linked inulin.

44. The pharmaceutical composition of Claim 43 wherein the active agent is absorbed into the cross-linked inulin.

20 45. A method of delivering an active agent to a patient comprising administering to the patient a pharmaceutical composition comprising an active agent and a cross-linked inulin characterized by a Degree of Substitution of at least about 10%, a Swelling Ratio at Equilibrium of at least about 2 and an average mesh size between about 10 and 100 Å.

25 46. The method of Claim 45 wherein the pharmaceutical composition is administered orally.

47. The method of Claim 46 wherein the active agent is absorbed in the intestine.

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48. The method of Claim ⁴⁶₄₇ wherein the active agent treats inflammatory bowel disorder or Crohn's disease.

5 49. A method of conducting an enzymatic reaction in anhydrous DMSO comprising contacting one or more enzymatic substrates solubilized in DMSO with an alkaline protease under reaction conditions thereby conducting an enzymatic reaction.

10 50. The method of Claim ⁴⁸₄₉ wherein the alkaline protease is Proleather.

51. The method of Claim ⁴⁸₄₉ wherein the enzymatic substrates include a polysaccharide and an acyl donor.

15 52. The method of Claim ⁵⁰₅₁ further comprising recovering an acylated polysaccharide from the reaction medium.

53. The method of Claim ⁵⁰₅₁ wherein the polysaccharide is selected from the group consisting of inulin and dextran.